Hospital-Based Descriptive Study of Symptomatic Hyponatremia in Elderly Patients

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Abstract

Background: Hyponatremia is a common electrolyte disturbance in the hospitalized elderly sick patients. There is no existing record for profiling of symptomatic hyponatremia in elderly Indian subjects.

Objectives:
- To study clinical features and etiology of hyponatremia in elderly hospitalized patients
- To classify severity of hyponatremia in hospitalized elderly

Methods: All elderly patients admitted to ICU with serum sodium level <= 125 mmol/L were included in study

Results: 100 patients with symptomatic hyponatremia (serum sodium <= 125 mmol/L) were studied. The CNS symptoms included drowsiness, lethargy, confusion, seizures and coma. There was female preponderance of cases (55%). The common co-morbid conditions were Hypertension (69%) and diabetes mellitus (51%). Females tolerated hyponatremia better than males with mortality of 9.09% in females and 33.33% in males (p=0.0026). The common cause of Hyponatremia was SIADH (30) followed by drugs of which diuretics was the major contributor.

Conclusion: Hyponatremia was more common in females and they seemed to better tolerate it than their male counterparts. Diuretics should be used with caution in elderly.

Introduction

Disorders of sodium and water metabolism are common in hospitalized patients and are occasionally encountered in outpatients. Both hyponatremia and hypernatremia can cause substantial morbidity and mortality, and ironically, incorrect treatment can add to the problem.

Hyponatremia is defined as a serum sodium concentration of less than 135 mEq per L. Patients with clinically significant hyponatremia present with nonspecific or neurologic symptoms attributable to cerebral edema. When coupled with a recent history of altered fluid balance, these symptoms suggest the possibility of hyponatremia, which can cause substantial morbidity and mortality.

Studies suggest that hyponatremia may be present in 15 to 22% percent of patients in chronic care facilities when serum sodium is defined as less than 135 mEq/L. The incidence is much more in the elderly mainly owing to impaired ability to maintain water and electrolyte homeostasis in response to dietary and environmental changes. The management of these cases needs modification due to physiological changes with age affecting the renal and other systems.

Data regarding the incidence of hyponatremia in elderly in our country is limited. This study was done to know the common clinical features and etiology of hyponatremia in elderly hospitalized patients and to correlate the outcome of these patients with admission serum sodium levels.

Materials and Methods

The study was done between 1st of April 2007 and 31 of October 2008 in our institution. Elderly patients (60 yrs and older) admitted in Medical Intensive Care Unit (ICU) with admission diagnosis of symptomatic hyponatremia (serum sodium <= 125 mmol/L) were included in the study. Relevant history including symptoms and signs at presentation, past medical history, drug history and examination findings were noted. Volemic status of the patient was assessed by examination. Routine blood and urine investigations including complete blood count, renal function tests, electrolytes, liver function tests, serum osmolality, urine routine, urine osmolality, chest radiograph and imaging studies were done to rule out other co-morbid conditions. Serum cortisol level and Serum T3, T4 and TSH were done when indicated. All patients were treated for hyponatremia based on the hospital protocol.

Sodium concentrations were measured on the Dimension RxL Max Integrated Chemistry System (Siemens India Inc.). This apparatus uses ion-specific electrode technique ensuring measurement of true hyponatremia. The normal range of the Laboratory for sodium is 135-145 mmol/L.

Serum and urine osmolality was measured on Osmometer 800 CL (Slamed Inc.). The apparatus uses freezing point depression technique for measuring osmolality. The normal range for serum and urine osmolality is 275-293 mOsm/Kg H2O and 500-850 mOsm/Kg H2O respectively.

Statistical Analysis

Excel (Microsoft Office 2007) and SPSS (SPSS inc, Chicago) software packages were used for data entry and analysis. The student ‘t’ test was used to determine whether there was a statistical difference between improved and expired subjects in the parameters measured. Proportions were compared using Chi-square test of significance. One way analysis of variance was used to test the difference between groups. In all the above test “p” value of less than 0.05 was accepted as indicating statistical significance.
Results

Of the total of 1440 elderly patients admitted to the medical ICU during the 18 month period, 518 patients (36%) had serum Sodium<135 mmol/L and 100 patients (6.9%) had serum Sodium <= 125 mmol/L. The mean age of patients with hyponatremia in our study was 72 years with a range of 60 to 99 yrs. 35 patients were females and 45 patients were males with preponderance of hyponatremia in elderly sick females. The mean sodium level on admission was 113.89 mMol/L and after correction was 129.54 mMol/L.

Lethargy, drowsiness with slow response and irrelevant talk were the common presenting symptoms in our study (Figure 1). Since the CT scan done for these patients showed no structural abnormality, these symptoms were attributed to hyponatremia. Some of these patients also presented with other non-CNS symptoms such as pain abdomen, decreased appetite which could not be accounted by hyponatremia.

At admission, 61% were euvolemic, 23% were overloaded and 16% dehydrated. The commonest type of hyponatremia noted in our study was Isovolemic Hypo-osmolar hyponatremia (Figure 2). There was no significant difference when the type of hyponatremia was analyzed with the outcome (p > 0.2559).

The common co-morbid conditions were Hypertension (62%), diabetes mellitus (51%), renal failure (22%) and ischemic heart disease (18%). The common causes of hyponatremia were SIADH (30%) followed by Drugs (24%), Frusemide (17%), Mannitol (3%), Metazolone (2%) and Cisplatin (2%) were the drugs found to be associated with drug induced hyponatremia (Fig. 3). None of the subjects were on Diuretics when SIADH was found to be the cause of hyponatremia.

20 patients succumbed to their primary illness with possible significant contribution secondary to hyponatremia. Female patients tolerated hyponatremia better with a mortality of 9.09% as compared to males with a mortality of 33.33%.

Though 33% of the patients with an admission serum sodium levels <105 mmol/L succumbed to death compared to 17.5% in those with admission serum sodium level between 105-125 mmol/L, there was no statistically significant difference between the two groups (p=0.1635).

Discussion

This study was undertaken keeping in view of frequent occurrence of hyponatremia in the elderly sick patients who are at higher risk of development of electrolyte disturbance as these people have age related physiological changes in the function of kidneys and other multiple co-morbid conditions.

The prevalence was more in females compared to males in our study. Chronic hyponatremia in postmenopausal women is common. Studies have shown that female gender is an important risk factor for the development of severe complications.60% of the cases in a prospective study on hyponatremia by Clayton et al were females.

Increased intracranial space due to naturally occurring age-related brain atrophy is known to play an important role in brain adaptation to hyponatremia in postmenopausal females. There is evidence to support the idea that adaptation of the elderly female rat brain to hyponatremia is largely dependent on physical factors (i.e., brain-to-skull size ratio). This finding suggests that even in the presence of cerebral edema, if the brain is able to swell without generating a significant increase of intracranial pressure, the prospects for patient survival may be substantially improved.

Only 4% of the total patients presented with seizures in the present study. Studies have shown that both aging and male gender confers protection against hyponatremia induced seizures, although the reasons are unclear.7

Most of the patients in our study had multiple co-morbid conditions of which hypertension and diabetes were the most common. Glucose being an osmotically active molecule, hyperglycemia can induce a fall in serum sodium levels by shifting water from intra-cellular to extra-cellular compartments. It has been calculated that serum sodium falls by 1.6 to 2.4 mmol/L for every 5 mmol/L rise in serum glucose levels.8

Hyponatremic hypertensive syndrome is a well known entity, the most common association being in patients with essential hypertension receiving diuretics. Most of the hypertensive patients in our study group were on thiazide or thiazide-potassium sparing diuretics which are known to interfere with metabolism of various electrolytes and predispose them to electrolyte imbalance. Along with their effect on sodium-chloride co-transporter channel, thiazide diuretics are known to cause non-osmotic release of vasopressin.10

SIADH was the most common cause of hyponatremia in our
study. Nearly half the patients with severe hyponatremia had SIADH in the study done by Clayton et al. Laczi reported that SIADH was the most common cause of euvolemic hyponatremia in their study in Hungary.\textsuperscript{11}

Of all the etiologies, the worrisome cause is Drug induced hyponatremia of which a major chunk was diuretics. Many studies have reported that drugs especially thiazide diuretics are a major cause of hyponatremia in elderly.\textsuperscript{3,4,12,13} Though JNC VII recommends diuretics as the first line drug for treatment of hypertension, a word of caution should be maintained while prescribing diuretics in the elderly and when required doses should be modified according to body weight and should begin with the lowest dose.

Many studies in the past indicate a higher mortality in the elderly patients with severe hyponatremia, with mortality ranging from 33\% to 86\%.\textsuperscript{14} In the present study the mortality rate was 20\%. Sterns reported a mortality rate of 5\% when the serum sodium levels was <105 mmol/L.\textsuperscript{14} When the mortality outcomes were compared with respect to gender distribution it was noticed that females though had higher incidence of hyponatremia, responded better to treatment compared to males with hyponatremia (p=0.0026). Among those who succumbed, the cause of death was secondary to severe sepsis or other conditions like progressive cerebro-vascular disease, advanced malignancy and acute coronary event. The association of hyponatremia with these patients could be incidental or secondary to the medications used by these patients for their pre-existing illness, as even those patients who succumbed to their illness had received correction for hyponatremia as per the standardized regimen of treatment followed in this study. Baran et al reported in their study that the association of hyponatremia and outcome was not causal; rather it appears to be a marker of an underlying disease which carries poor prognosis.\textsuperscript{15}

**References**

1. Janicic N, Verbalis JG. Evaluation and management of hypo-
11. Laczi F. [Etiology, diagnostics and therapy of hyponatremias] [Article in Hungarian]. *Orv Hetil* 2008;149:1347-54.